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Procedia Computer Science 96 (2016) 1075 – 1085

Procedia Computer Science

20th International Conference on Knowledge Based and Intelligent Information and Engineering Systems

The Changing Structures of Co-invention Networks in American Urban Areas

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Abstract

Theories of localized knowledge exchange argue that proximity among economic actors in spatial clusters fosters invention and innovation. An alternative perspective stresses collaborative networks in which individuals and groups are embedded in wide-ranging webs of social relationships. This study uses social network analysis to explore the changing structures of co-invention networks in American urban areas from 1979 to 2009. Results show that inter-urban network complexity has broadened and deepened. A dense web of knowledge exchange has emerged that is not singularly controlled by a handful of intermediaries. National linkages have developed, but intense local and regional ties persist. Inventors in small areas are obliged to substitute inter-urban networks for thin agglomerative economies. The co-invention system approximates a core-periphery structure with core urban areas strongly tied to one another and to peripheral areas. Inventors in less consequential peripheral areas rely on the core for collaborative connections.

Peer-review under responsibility of KES International

Keywords: Networks; Knowledge exchange; Co-invention; Co-patenting; Biotechnology

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Peer-review under responsibility of KES International
doi:10.1016/j.procs.2016.08.132

1. Introduction

Geographical concentration of economic actors in clusters enhances interpersonal interaction and communication, labor mobility, and research collaboration [1, 2]. Spatial clusters of invention and innovation, tied to localized knowledge flows in and among the cities and regions of the US and Europe, have been extensively documented [3, 4, 5, 6, 7, 8]. Knowledge flows also circulate in wide-ranging collaborative networks via social relationships and linkages [9, 10, 11, 12]. In successful collaborative networks, people exchange information, develop vicariously perceptions and opinions, and reduce uncertainty about events, ideas, or phenomena in pursuit of particular goals [13]. Collaboration increasingly spans long distances [10, 14]. Network-based proximity links scientists and engineers in different cities, especially in dynamic technologies such as biotechnology where research collaboration has become crucial for inventive performance [15, 16, 17, 18, 2]. Combining complementary local and non-local skills and competences are essential for rapid adaption in fast changing technological environments [19, 20, 21, 22, 17, 23]. This article illuminates the structural properties of the US co-invention network over time. The central goal is to figure out the changing strength of both national linkages and regional biases in inter-urban collaboration.

I focus on co-invention networks of biotechnology patenting because technological advance in this field involves the deepening of collaboration and the broadening of inventor relationships [24, 25, 26, 27, 28, 17, 18, 10]. Networks are constructed by tracking inventors who participate in co-patenting in 1979 and 2009 and attributing each co-patent to urban areas where the inventors reside. Investigating specific structural properties of the networks helps answer the following interrelated questions. Are closely connected groups of areas evident in the system, are some groups more critical than others, are the groups national of regional, and are the groups stable over time? What are the pivotal metropolitan areas, are centrality rankings stable, and is an area's level of centrality in the system positively associated with its inventive performance? As collaboration grows, has enhanced complexity allowed knowledge flows to follow more routes? Finally, does a core-periphery arrangement accurately describe the system in 2009 or has broader collaboration erased such distinctions?

2. Knowledge exchange between inter-urban networks

Considerable research effort has been made to identify the nature and strength of localized knowledge exchange by showing that higher rates of research and development, invention and innovation, entrepreneurial activity, and high-technology production are bounded in space [3, 4, 5]. Other studies increasingly stress that access to external knowledge is also critical to triggering successful innovation and regional development [10, 15]. Breschi and Malerba [29] argued that strong external links vital regional competitive advantages. Bathelt [1] showed that dynamic firms in successful clusters by building and maintaining a variety of internal and external knowledge resources. In addition, advanced information and communication technologies reduce costs of moving knowledge and increase access and availability of universal resources [17]. The concepts of extra-local links and external knowledge resources provide new ways for explaining the geography of invention and innovation. Technological and commercial successes of many firms in Silicon Valley, for example, are closely tied to partners located in other regions and countries [18].

Innovation and invention not only require local interaction between nearly firms, but they also need ties among distant partners that provide access to complementary information, skills, and technologies [10, 12, 13]. Knowledge flows are no longer tightly bundled within a given geographical boundary. The spatial pattern functions as a network-based system associated with different geographical sites. A framework of inter-urban co-invention networks is proposed here with an emphasis on biotechnology patenting for the following reasons. First, intense invention and innovation is particularly significant in biotechnology. A large portion of biotechnology value-chains occurs in few global centers such as Boston and San Francisco in North America, and Cambridge, Munich, and Stockholm in Europe [19]. Second, the circulation of knowledge through non-local links provides a diversity of exchange opportunities for local learning and invention. Individual areas link to and integrate with a global network-based system. Each area has a distinctive knowledge architecture that supports local clients and customers, but they also provide markets and economies of scale for firms whose activities span multiple distant locations [10]. Successful networking strategies assist in accessing external knowledge. Most remote firms crucially rely on global networks [20].

Figure 1 links the interface between an inter-urban networks and its knowledge circulation. The upper part of the figure shows a simple geographical space with areas A to F. The actors are urban areas with co-invention connections. The lower part of the figure illustrates its social network counterpart, as individual inventors are located in different areas. The links in the lower part refer to co-inventive activities between individual inventors. Some inventors have extra-local relationships with inventors located in other areas, while some inventors only collaborate with other local partners. Co-patenting is viewed as evidence of groups of inventors participating in cooperative invention activities. Inventor ties shape the inter-urban network shown in the upper part of the figure. Area C, for example, is directly connected to A, D, and E, indirectly connected to B, and it has no connection with F.

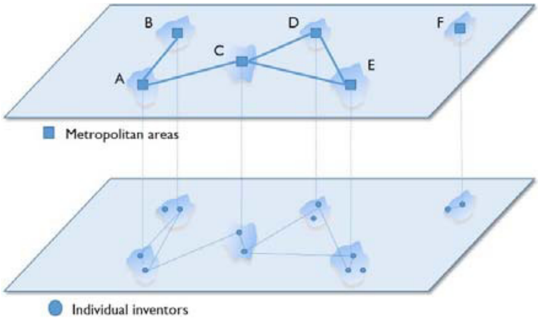

Figure 1. Inter-urban network of co-invention and knowledge exchange

3. Methodology

This analysis of the changing structures of co-invention networks emphasizes co-patenting ties formed by inventors, but ascribes their connections to the US urban areas where they reside. While I assume that urban areas share knowledge through co-patenting and that each area has a competitive niche that is integral to the network, the paths I sketch are rudimentary proxies or mere glimpses into knowledge exchange that occurs in collaborative encounters. Alderson, Bechfield, and Sprague-Jones [30] developed a corresponding investigation of the urban hierarchy through analysis of the locations of large firms' headquarters and subsidiaries. Detailed descriptions of the methods used below are available in Wasserman and Faust [31], Scott [32], Borgatti et al. [33], and Knoke and Yang [34].

3.1. Network components and cohesive subgroups

The first task is to identify components and cohesive sub-groups of inter-urban co-invention networks in 1979 and 2009. A component is a connected set of nodes (urban areas) with either direct or indirect links to each other. A cohesive sub-group is a subset of a component with relatively strong or frequent ties [31]. Two traits identify cohesive sub-groups -- the number of neighbors of each node and the frequency of connection between each nodal pair. The former is entitled the k-cores and the later the m-slices procedure [32, 34]. Identification of cohesive sub-groups permits addressing several interrelated questions. Is the core of the network structured into sub-groups focused on certain pivotal centers? Do members of sub-groups have distinctive geographical settings? Do metropolitan areas vary in connection intensity and are these connections stable over time?

3.2. Network centrality

The second task is to assess the extent to which a whole network has a centralized structure. Scott [32] and Knoke and Yang [34] outlined several global-level measures of social network that I use to reveal the centrality of a co-invention network by emphasizing the central interrelated questions: How tightly organized is the network around its most central area(s)? and is the level of overall centrality stable over time? Network centrality is generated by calculating the variability of all individual nodes' centralities around the one with the largest centrality. The measure of network centrality has degree, closeness, and betweenness properties.

Network degree assesses the extent to which an entire network has a centralized structure. Scores range from zero and unity. A zero value occurs in a regular graph where each node has the same degree. The maximum value of unity occurs in a star graph as all areas tie to one center. **Network closeness** examines assesses the variability of all nodes' closeness centralities around the largest closeness centrality. The minimum value of zero occurs in a regular graph, while the maximum value of unity occurs in a star graph. Large values occur when a few urban areas are highly central, and the rest occupy less pivotal positions. **Network betweenness** is the variability of all nodal betweenness scores around the largest betweenness score. The maximum value of unity when a single dominant node sits on all geodesic paths in a star graph. The minimum value of zero occurs when every node has the same betweenness score. The closer a network betweenness approaches one, the more unequally distributed is betweenness-based centralized in a network.

3.3. Nodal centrality

The third task is to examine the local-level properties of a co-invention network by identifying the pivotal urban areas. Specific questions addressed include the following: How important is an urban area in transferring knowledge to other areas? To what extent does an urban area control or mediate knowledge exchange in the network? Are centrality-based rankings of areas stable?

Nodal degree tallies the number of direct ties an individual has with all others. Scores range from zero to unity. A zero value occurs if node i has no connection with another node. If node i is directly tied to all g-1 other nodes, the maximum value is unity. This measure is straightforward in measuring and comparing nodal centrality. The network center is simply the metropolitan area with the most direct connections. **Nodal closeness** assesses knowledge exchange through both direct and indirectly connections. It is an inverse function of the geodesic distances from a given node to all others. An area with a high nodal closeness is critical in facilitating knowledge across the network. Nodal closeness requires a focus on the main component with the exclusion of isolates and subcomponents. **Nodal betweenness** calculates the extent to which an area is located on geodesic paths connecting other areas. A geodesic path between two areas is the shortest and most efficient channel for transferring knowledge. If more than one geodesic path links two areas, paths with the same number of segments are equally likely to be selected. Relatively large values identify gatekeepers of information exchange.

3.4. Core-peripheral hypothesis

The final task is to test relationships between groups of urban areas in 2009. These groupings are termed network positions of nodes that have similar patterns of relationships with the rest of the system [31]. Network positions help evaluate the hypothesis that the inter-urban co-patenting network is consistent with a core-periphery structure [35]. The questions I addressed include: do groups of areas have similar network positions? How do positions interrelate? Is a core-periphery structure evident?

The regular equivalence criterion partitions individual areas into network positions. This approach identifies nodes with similar patterns of ties to other equivalent nodes [31, 34]. Figure 2 shows a conceptual graph with three regular equivalent positions: {A}, {B, C, D}, and {E, F, G, H, I}. Nodes E, F, G, H, and I are regularly equivalent because they have no tie with any node in the position {A}, but all have a direct tie to the position {B, C, D}. I use White and Reitz's [37] regular graph equivalence (REGE) algorithm to estimate the degrees of regular equivalence for pairs of urban areas. The REGE algorithm is iterative and a three-round iteration REGE algorithm is the default in the UCINET software that I choice. I use hierarchical clustering to identify patterns of similarity by grouping urban areas' network positions with similar degrees of regular equivalence. A tree diagram or dendrogram depicts the hierarchical results and inspection permits the identification of positions.

A blockmodeling approach to characterize the relationship between the positions. A *priori* justification is used to associate positions with either the core or periphery. The term *block* refers to a square submatrix of regularly equivalent urban areas that have similar ties [31, 34]. A block filled with "1s" is titled *1-block*, while a block of solely "0s" is titled *0-block*. In a standard core-periphery model, the core-core submatrix is a 1-block of ties, meaning each core area has a ties with all other core areas. In contrast, the periphery-periphery submatrix is a 0-block of ties, showing no ties between peripheral areas. The two core-periphery submatrices representing ties between core and peripheral areas can be either 1-block or 0-block. Two idealized versions of pattern matrices that correspond to the core-periphery interaction are fashioned [35]. Figure 3 shows the first idealized pattern matrix where ties fully and only exist in both the core-core and the core-periphery blocks (1-blocks) and are absent in the periphery-periphery block (0-block). In an alternative idealized version of the pattern matrix, ties only exist in the core-core block (1-block) and are absent in the other blocks (0-blocks). These two idealized pattern matrices are compared with the 2009 co-invention matrix of inter-urban ties. The cells of the latter are converted to binary values with 1s and 0s showing the presence or absence of a connection, respectively. The Quadratic Assignment Procedure (QAP) correlates the strength of the relationship between each idealized binary pattern matrix [35], which I use to test the hypothesis that the binary co-invention matrix in 2009 has a core-periphery structure.

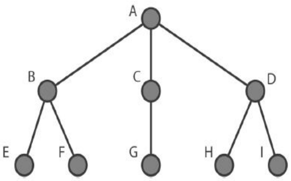

Figure 2. Conceptual graph of equ

		Core				Periphery					
		1	2	3	4	5	6	7	8	9	10
Core	1		1	1	1	0	0	0	0	0	0
	2	1		1	1	0	0	0	0	0	0
	3	1	1		1	0	0	0	0	0	0
	4	1	1	1		0	0	0	0	0	0
Periphery	5	0	0	0	0		0	0	0	0	0
	6	0	0	0	0	0		0	0	0	0
	7	0	0	0	0	0	0		0	0	0
	8	0	0	0	0	0	0	0		0	0
	9	0	0	0	0	0	0	0	0		0
	10	0	0	0	0	0	0	0	0	0	

		Core				Periphery					
		1	2	3	4	5	6	7	8	9	10
Core	1		1	1	1	1	1	1	1	1	1
	2	1		1	1	1	1	1	1	1	1
	3	1	1		1	1	1	1	1	1	1
	4	1	1	1		1	1	1	1	1	1
Periphery	5	1	1	1	1		0	0	0	0	0
	6	1	1	1	1	0		0	0	0	0
	7	1	1	1	1	0	0		0	0	0
	8	1	1	1	1	0	0	0		0	0
	9	1	1	1	1	0	0	0	0		0
	10	1	1	1	1	0	0	0	0	0	

Figure 3. Idealized core-periphery pattern matrix (the first version on the left, the alternative version on the right)

4. Data and observations

Aspects of biotechnology knowledge exchange are encapsulated in patent co-invention, which occurs when a patent has more than one inventor [27, 28]. I follow Hall et al. [38], Cortright and Mayer [25], and Hevesi and Bleiwas [36] in using US patent classes 424, 435, 514, and 800 to define biotechnology. Classes 424 and 514 are drugs, particularly bio-affecting and body-treating compositions. Class 435 is a chemical grouping and includes molecular biology and microbiology inventions. Class 800 encompasses multicellular living organisms, unmodified parts thereof, and related processes. Patents in these classes in 1979 were extracted from the National Bureau of Economic Research (NBER) databases. The 2009 data were provided by the USPTO [39].

The geographical units in each year are the Metropolitan Statistical Areas defined in the intermediate year of 1999. Owing to the uneven distribution of biotechnology patents across the country, small urban areas without any co-patented awards are discarded. This sidesteps swamping the analysis with cases that have no co-patenting and the likelihood that they would be mistakenly identified as outliers. The number of observations is reduced to 150 large urban areas that had at least one biotechnology co-patent awarded in 1999.

Patents generated by multiple are distinguished from those by solo inventors. Each patent must have at least one inventor located in one of 150 large US urban areas. Foreign partners are ignored. I specify the geography of biotechnology co-patenting by attributing each co-patent to the urban areas where the inventors reside. Co-patents with inventors living in multiple areas are allocated fractionally, which corresponds with Maggioni et al. [10] and Ejermo and Karlsson [40]. If a co-patent has four inventors located in four different urban areas, one-quarter of the co-patent is allotted to each area. The website of US Bureau of Economic Analysis provided the job data.

The number of US biotechnology patents is large and growing—from 883 in 1979 to over 6,356 in 2009. Co-patenting increased faster—from 55% to 81% of biotechnology awards. Average team size increased from 2.54 co-inventors in 1979 to 4.07 in 2009. Table 1 shows the geographical reach of biotechnology co-patenting across the 150 large urban areas. Most co-patenting occurs within the same area, but the trend reveals increasing interconnected collaboration—from 17% in 1979 to 38% in 2009. Moreover, a growing number of urban areas jointly participated in co-patenting, leading to a wider network of collaboration. In 1979, co-patenting never stretched beyond three urban areas, but by 2009, a handful of co-patents tied inventors of five and more areas. In short, knowledge collaboration in biotechnology advance is deepening and broadening across the geographical boundary.

Table 1. Biotechnology co-patenting, percentage intra-urban and inter-urban areas, 1979 and 2009

	1979	2009
Intra-urban area (co-patenting in the same area)	83.2%	62.3%
Inter-urban areas (co-patenting with a different urban area)	16.8%	37.7%
Co-patenting across two urban areas	16.3%	30.0%
Co-patenting across three urban areas	0.5%	6.7%
Co-patenting across four urban areas	0.0%	0.8%
Co-patenting across five urban areas (and above)	0.0%	0.2%

Sources: Hall et al. [38], US Patent and Trademark Office [39]

5. Results

5.1. Network components and cohesive subgroups

The structure of co-invention network is presented by identifying components and the strongest subgroups of the largest one. Figure 4 shows the 1979 network of nodes and pairwise co-invention ties. The width of a line segment is set by the frequency of co-patenting, indicating the strength of collaboration between each urban pair. 107 isolated urban areas do not co-invent with another area that are not displayed. The 1979 co-invention network exists seven components by directly or indirectly connecting with other nodes. The largest component consists of 29 urban areas. Figure 5 shows the densest part of the 1979 co-invention network. The strongest cohesive subgroup consists of 15 areas that are directly tied to at least two other areas, particularly, New York and Philadelphia have the closest direct connections with 17 co-patenting ties. Other areas in the cohesive subgroup only have two co-patenting ties. Most connections are intra-regional. New York and San Francisco, for example, have only one tie. The 83% of co-invention occurring in the same area with accompanying regional bias in the densest part of the network shows that local and regional relationships characterize the 1979 inter-urban co-invention network. Mainly local interactions and inter-urban connections occur within their regional centers.

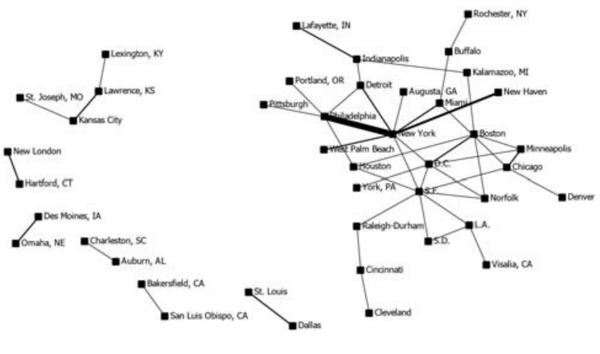

Figure 4. Inter-urban co-invention network, 1979

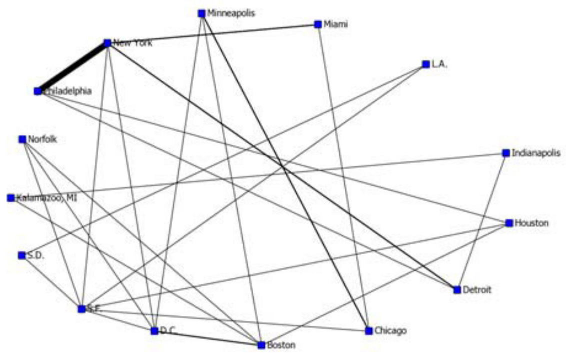

Figure 5. Densest part of the 1979 iInter-urban co-invention network

The 2009 co-invention network has a much denser web of inter-urban relationships with a main component of 138 areas, as shown in Figure 6. No other small components occur. Co-patenting ties increased to 887 and multiple strong national-level connections are evident. San Francisco, collaborating with 75 partners, replaced New York (69 partners) as the leading center. Boston, San Diego, and Los Angeles also function as national-level centers with 66, 64, and 60 partners, respectively. Figure 7 shows the densest cohesive subgroup consisting of 26 areas that have at least 13 partners. Several robust linkages are national. Inventors in San Francisco collaborate with partners in New York (47 ties), Boston (45 ties), Philadelphia (37 ties), Washington (37 ties), Chicago (15 ties), Denver (13 ties), Des Moines (12 ties), New Haven (12 ties), and Raleigh-Durham (10 ties). Beyond strong connections with San Francisco, New York's inventors have robust connections with San Diego (19 ties) and Los Angeles (18 ties). Seattle's inventors collaborate with partners in Boston (8 ties). Los Angeles has strong links with Boston (32 ties) and Chicago (10 ties). The university towns of Tucson (AZ) and Raleigh-Durham have 12 co-patents. Examples of lesser national level ties include connections between State College (PA) and Corvallis (OR), Richland (WA) and Miami (FL), and Johnson City (TN) and Portland (OR).

The geography of co-invention in 2009 clearly has essential national attributes, but strong regional affinity endures. In the Northeast Corridor, New York has robust links with Philadelphia (162 ties), Boston (65 ties), New Haven (46 ties), and Washington D.C. (24 ties). Philadelphia is strongly connected with Boston (36 ties) and Washington D.C. (23 ties). In the Pacific Coast region, intense collaboration occurs between San Francisco and San Diego (78 ties), followed by San Francisco and Los Angeles (64 ties). Seattle and Sacramento also belong to this alignment. Persistent regional bias, with 62% of collaboration occurring exclusively at the intra-urban level, indicates that distance sensitive knowledge exchange remains vital in biotechnology advance.

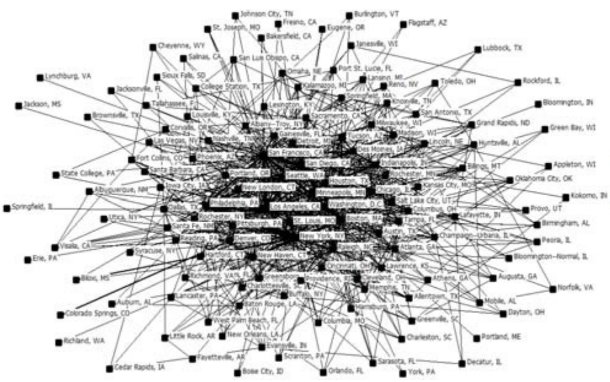

Figure 6. Inter-urban co-invention network, 2009

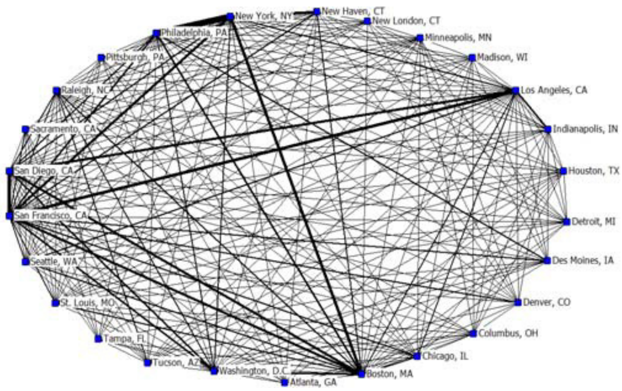

Figure 7. Densest part of the 2009 inter-urban co-invention network

5.2. Network centrality

Three global-level measures of network centrality—degree, closeness, and betweenness are computed to ascertain the tightness of co-invention networks in 1979 and 2009. The results show that the 2009 co-invention network has the highest network degree with a score of 0.460, while in 1979 the network degree was 0.204. As patenting increased and co-patenting intensified in biotechnology, knowledge exchange expanded across the US geography. The network closeness, which includes both the direct and indirect ties, increased from 0.348 to 0.449 as enhanced deepened system-wide connections. The network betweenness declined, from 0.400 to 0.129. As network complexity increased, additional gatekeepers participated in controlling knowledge exchange. Major centers are more directly tied to other areas, but more collaboration allows biotechnology knowledge to follow alternative routes.

5.3. Nodal centrality

Table 2 lists the top 15 urban areas ranked by individual's nodal degree, closeness, and betweenness. By 2009, San Diego and Seattle in the west, St. Louis and Madison in the midwest, Atlanta in the south, and New Haven and Raleigh-Durham in the east all had replaced Detroit, Miami, Houston, Norfolk, Minneapolis, Buffalo, and Cincinnati in the top 15 urban areas ranked by nodal degree. These centers rising in the 2009 ranking list regarding nodal degree and nodal closeness contain major research universities, strong technological infrastructure, and entrepreneurial cultures. The 2009 ranking list of nodal betweenness is similar to the lists of nodal degree and closeness. Most discrepancies are minor, although New Haven's absence from the betweenness top 15 contrasts with its 12th position in closeness. The 1979 rank discrepancies across the three measures are wider suggesting that by 2009 the co-invention network had matured with the magnitude of areas' direct and indirect connections comparable. Particularly, nodal betweenness shows the most skewed in both years of analysis, but dominance at the top waned as New York and San Francisco's scores declined. Nonetheless, both centers remain situated on the geodesic paths between many urban areas and are crucial to information exchange through the network across the space. The pivotal centers, with Boston, San Diego, and Los Angeles, served as go-betweens for areas not directly tied. Across all measures of nodal centrality, these five centers are critical in the contemporary American biotechnology co-invention network.

Table 2. Top 15 urban areas by measures of nodal centrality, 1979 and 2009

Nodal degree		Nodal closeness		Nodal betweenness	
		Year of 1979			
San Francisco	0.286	New York	0.500	New York	0.464
New York	0.286	San Francisco	0.483	San Francisco	0.447
Washington, D.C.	0.214	Washington, D.C.	0.444	Miami	0.160
Boston	0.179	Houston	0.394	Philadelphia	0.154
Philadelphia	0.179	Philadelphia	0.389	Washington, D.C.	0.146
Chicago	0.143	Detroit	0.384	Raleigh-Durham	0.138
Detroit	0.107	Chicago	0.384	Chicago	0.128
Miami	0.107	Miami	0.378	Detroit	0.117
Houston	0.107	Boston	0.373	Boston	0.088
Norfolk	0.107	Norfolk	0.368	Indianapolis	0.087
Minneapolis	0.107	Minneapolis	0.359	Cincinnati	0.071
Indianapolis	0.107	Raleigh-Durham	0.346	Los Angeles	0.071
Los Angeles	0.107	Los Angeles	0.341	College Station	0.071
Buffalo	0.071	San Diego	0.337	Houston	0.066
Cincinnati	0.071	West Palm Beach	0.337	Kalamazoo	0.028
		Year of 2009			
San Francisco	0.547	San Francisco	0.688	San Francisco	0.137
New York	0.518	New York	0.675	New York	0.130
Boston	0.482	Boston	0.656	Boston	0.099
San Diego	0.467	San Diego	0.643	San Diego	0.099
Los Angeles	0.438	Los Angeles	0.637	Los Angeles	0.079
Washington, D.C.	0.431	Philadelphia	0.628	Washington, D.C.	0.076
Philadelphia	0.423	Washington, D.C.	0.623	Philadelphia	0.066
Raleigh-Durham	0.328	Raleigh-Durham	0.585	Chicago	0.042
Chicago	0.314	Chicago	0.578	Indianapolis	0.039
Seattle	0.292	Seattle	0.573	Raleigh-Durham	0.036
St. Louis	0.27	St. Louis	0.564	Seattle	0.035
Indianapolis	0.226	New Haven	0.555	Madison	0.030
Madison	0.226	Madison	0.548	Atlanta	0.025
New Haven	0.219	Indianapolis	0.548	Dallas	0.022
Atlanta	0.212	Houston	0.539	Denver	0.019

Source: Hall *et al.*[38], USPTO [39]

5.4. Core-peripheral hypothesis

The U.S. biotechnology co-invention network in 2009 is assumed to consistent with a core-periphery structure by following the two specific phenomena: (1) core areas that are essential to the network with strong connections to each other and to outsiders, and (2) peripheral areas that play less consequential roles as they are loosely connected or even disconnected from one another, but are mostly connected with core areas. I investigate this hypothesis using regular equivalence to partition 138 individual urban areas located in the main component of the network via hierarchical clustering into five network positions, as shown in Table 3.

San Francisco and New York form Position 1, entitled the *primary* areas have similar connections in the network with tied to over 70 other urban areas. The second equivalent position contains 38 urban areas including Boston, Philadelphia, Indianapolis, San Diego, Chicago, Seattle, and Washington D.C., titled the *major* areas. Their connections in the network are mutually collaborative—approximately 55% of their co-patenting ties (277 of 504) are with members of the position. Nine urban areas from the third equivalent position, entailed the *regional* areas.

With limited co-patenting activities, these areas, included Albuquerque, Buffalo, Santa Barbara, and Santa Fe, only have 13% of the inter-urban ties (5 of 38) that are internal to the position. Fifty-eight urban areas form the *minor* areas. These areas are less connected with each other and the proportion of internal ties is less than 18%. The last equivalent position consists of 31 urban areas that titled the *outskirt* areas. In a core-periphery structure, these areas are isolated from one another and they have the lowest nodal centrality scores, which are arrayed on the periphery. Their connections more frequent occur with areas located in the central positions.

A *priori* justification is used to associate positions with either the core or periphery. I assume that both the primary the major areas comprise the core of the network because they are highly connected with each other. In contrast, the regional, minor, and outskirt areas comprise the periphery due to their ties mainly connect to the core, but not to each other. The QAP calculations show that the relationships between the binary co-invention matrix and both the idealized pattern matrices are statistically significant. In summary, core biotechnology centers are densely connected by co-patenting. A few peripheral urban areas have strong ties to the core centers, but they account for few of the connections in the 2009 inter-urban co-invention network.

Table 3. Characteristics of regularly equivalent position in 2009

Position name	Mean nodal degree	Mean nodal closeness	Mean nodal betweenness	Self-ties / All-ties
Primary areas (2)	0.533	0.682	0.134	1/73
Major areas (38)	0.194	0.535	0.022	277/504
Regional areas (9)	0.062	0.470	0.001	5/38
Minor areas (58)	0.057	0.457	0.002	41/226
Outskirt areas (31)	0.022	0.384	0.000	0/46

Measures of nodal centrality calculated from the 2009 main component (138 urban areas)
Self-ties = number of ties that members of the positions have with one another
All-ties = total number of ties of members of the position

6. Conclusions

This article provides insights into the network structure of knowledge flows in co-invention networks of American biotechnology. I track co-patenting ties in inter-urban networks to account for bilateral knowledge exchange between 150 US large urban areas. Results show that a thin network in 1979 that was largely fragmented and regionally focused became far more connected and better organized by 2009. While regional biases persisted, a national level space of knowledge flows emerged. The major component of the 1979 co-invention network consisted of 29 areas, while the inter-urban network in 2009 connected 138 areas. At the top of the 2009 nodal centrality, San Francisco and New York serve as national pivots. Other major centers including Boston, Los Angeles, Chicago, Philadelphia, San Diego, Washington D.C., and Seattle are less directly connected but they are important intermediaries. Dominance by a few areas corroborates Coenen et al. [26] and Cooke [18] claims that major centers are pivotal in open innovation systems that stretch knowledge domains over great distances. Third, some small and medium metropolitan areas have emerged as important gatekeepers of knowledge exchange. These nodes fall on the geodesic paths between many other areas in the network. Raleigh-Durham, Indianapolis, and Madison, for example, mediate knowledge flows to other areas. Gatekeepers increase opportunities for less pivotal areas to access knowledge.

Analysis of the co-invention network in 2009 supports a core-periphery depiction of the network. The core consists of 40 urban areas with relatively high levels of knowledge sharing and collaboration. The periphery contains 98 urban areas that play far less consequential roles. A core-periphery property is common in network structures and is not evidence of a flawed system of technological advance. Barabási [41] argued that networks often follow a trend of core reinforcement and eventual peripheral growth. Members of the core establish conventions and norms that encourage knowledge exchange, while those in the periphery constitute a pool of potential recruits that can bring fresh perspectives and alternative ideas to the system [42].

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